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A human nuclear protein with sequence homology to a family of early S phase proteins is required for entry into S phase and for cell division.

Todorov IT, Pepperkok R, Philipova RN, Kearsey SE, Ansorge W, Werner D.

Division of Cellular Biochemistry, German Cancer Research Center, Heidelberg.

Molecular cloning and characterisation of a human nuclear protein designated BM28 is reported. On the amino acid level this 892 amino acid protein, migrating on SDS-gels as 125 kDa polypeptide, shares areas of significant similarity with a recently defined family early S phase proteins. The members of this family, the *Saccharomyces cerevisiae* Mcm2 Mcm3p, Cdc46p/Mcm5p, the *Schizosaccharomyces pombe* Cdc21p and the mouse prote P1 are considered to be involved in the onset of DNA replication. The highest similarity was found with Mcm2p (42% identity over the whole length and higher than 75% over a conservative region of 215 amino acid residues), suggesting that BM28 could represent a human homologue of the *S. cerevisiae* MCM2. Using antibodies raised against the recombinant BM28 the corresponding antigen was found to be localised in the nuclei of various mammalian cells. Microinjection of anti-BM28 antibody into synchronised mouse NIH3T3 or human HeLa cells presents evidence for the involvement of the protein in cell cycle progression. When injected in G1 phase the anti-BM28 antibody inhibits the onset subsequent DNA synthesis as tested by the incorporation of bromodeoxyuridine. Microinjection during the S phase had no effect on DNA synthesis, but inhibits cell division. The data suggest that the nuclear protein BM28 is required for two events of the cell cycle, for the onset of DNA replication and for cell division.

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